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FOREWORD

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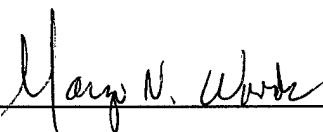
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in Women at High Risk for Breast Cancer
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Introduction:

The purpose of the study was to investigate the effects of consuming a soy protein bar, containing 45mg of phytoestrogens/day, on menopausal symptoms in women at increased risk for breast cancer using a double blind cross-over design. Soy protein and placebo bars were to be consumed daily for 3 months each, with a one month wash-out between treatments. Women reporting a high level of hot flashes, >5/day, were recruited and the number of hot flashes occurring daily were kept in a "symptoms diary" along with periodic evaluation of the severity of the hot flashes. Hormones were determined at baseline and at the end of each treatment period. A hundred women who were peri-menopausal or menopausal were sought for this aspect of the study. In addition a second group of women who reported low levels of hot flashes during menopause were also recruited to serve as a contrast group for hormonal levels and its association with menopausal symptoms, (N=50). A medical history and menopausal history were taken on all women.

Original Hypothesis:

The use of a soy dietary supplement bar in women at increased risk for breast cancer and reporting high menopausal symptomatology will result in a decrease in symptoms as well as alterations in endogenous hormone levels.

Specific Aims:

1. Recruit 100 menopausal women for the study who are experiencing frequent and consistent menopausal symptoms of hot flashes (>5 per day) and/or night sweats (>5 per week) to participate in an intervention study. Recruit 100 menopausal women without symptoms who will act as a control group in which only baseline data will be collected.
2. Use a randomized cross-over study design, in which women with high menopausal symptoms will be given a soy dietary supplement bar or a placebo bar for 3 months, with a wash out period of 1 month, followed by the alternative dietary intervention.
3. Collect data on menopausal symptoms using a daily symptoms diary for the duration of the intervention study.
4. Collect blood samples for determination of sex hormone levels on the women for two consecutive days at baseline, after three months of soy supplementation and after three months of placebo.
5. Collect a 24 hour urine sample for determination of phytoestrogens at baseline, after three months of soy supplementation and after three months of placebo.
6. Collect a food frequency questionnaire at baseline on all participants and 3 Day Food Records from the Intervention Group at baseline and at the end of each study phase, concurrent with the blood and urine collection.

Body:

Study Design:

A randomized double-blind study design was used to investigate whether the consumption of 45 mg of phytoestrogens per day, given via a dietary soy bar would decrease menopausal symptoms and endogenous hormones in post menopausal women, compared to the same woman

during consumption of a placebo dietary bar. Women were recruited into the study if they meet the eligibility criteria of being menopausal (ages 45-58), reported high levels of hot flashes (>5/day), and had not had a menstrual cycle in the last 6 months. Exclusion criteria included being on hormone therapy during the last 6 months, hysterectomy with loss of both ovaries, taking steroid medications, frequent use of antibiotics, currently consuming soy products >2/week.

The study protocol included a telephone screening and a two-week run-in with collection of baseline data on recording of number of hot flashes/day and serum for hormone determinations to determine eligibility. Those women who qualified began three months (Phase I) of consuming a study diet bar (soy or placebo) during which time they again kept daily record of hot flashes, consumption of dietary bars and determination of hormone levels in weeks 11 and 12. This was followed by one month of a wash-out period in which no study dietary bar was consumed. Phase II was the following 3 months with consumption of the alternative study bar (placebo or soy) and similar collections of data as in Phase I, with blood collected for hormone determinations in weeks 27 and 28. A small sub-set of the study population (N=7) were used to determine serum phytoestrogen levels to compare with levels reported in the Asian population.

A separate group of women designated Control Women were recruited with the same eligibility and exclusion criteria except they were reporting low levels of hot flashes (<1/day). Only baseline data were collected on this population. Forty-five women were recruited for this aspect of the study. Data are presented on only 32 of those women due to difficulty in the data analysis on the final group of 13, but complete data on the 45 will be available for the publication from this research.

A Menopausal Symptoms Questionnaire was collected on the intervention women as well as a 3 day food record at baseline, and at the end of Phase I and Phase II which have been entered into the data analysis software but preliminary analyses have not been completed.

The statistical analyses used for each of the comparisons is included on the tables presented and statistical work is still being carried out on this data set.

The research results will be presented as follows: 1) basic characteristics of the intervention study subjects, 2) number and intensity of hot flashes during study phases, 3) serum hormones by phase of study, 4) contrast of hormone values in women reporting low levels of hot flashes versus those reporting high levels of hot flashes, and 5) serum phytoestrogen levels in a sub-set of intervention subjects.

The data from the study is still being evaluated and the data presented address the specific aims outlined in the grant proposal. Additional questions will undoubtedly be investigated and analyzed, that will not be completed by the time this report is due. Additional data can be supplied as manuscripts are prepared. This preliminary data will be reported at the Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease, Washington, D. C., October 31-November 3rd.

Results:

Table 1 contains the demographic data on the subjects recruited for the soy intervention. A total of 95 subjects were recruited for the study, with 19 drop-outs, for a total of 76 completing the protocol. The data presented are on 76-79 of the subjects. The mean age of the population is

51.6 years of age with a mean weight of 63.6 kg. They reported a mean age at menarche of 12.4 years and age of menopause of 48.1 years. The intensity of hot flashes which was collected for 1 week at baseline indicates a significantly higher intensity of hot flashes in those reporting >5 hot flashes/day compared to those with <5 hot flashes/day at baseline (2.49 versus a score of 1.99, respectively, $p=0.0004$). Data on Socio-Demographic history and Reproductive History are included in Table 2. More women who reported <5 hot flashes/day were currently married ($p=0.05$) in this study population. There were no other differences in reproductive history in women reporting different levels of hot flashes (>5/day versus <5/day). Approximately 70% of the women reported they had used oral contraceptives and approximately 35% reported they ever used HRT for menopause.

Table 3 includes the data on the mean number of hot flashes/day for the women ($N=76$) at baseline, and while on the soy or placebo bar. Compared to baseline, both the placebo and soy bar show a significant decrease in reported number of hot flashes ($p=0.0001$). When the soy bar is compared to the placebo bar, there is no significant difference ($p=0.32$). Note that we have 973 observational days at baseline, 6369 days on the soy bar, and 6278 days on the placebo bar. Looking at this same data as a percent change from baseline according to bar type, Table 4 shows that compared to baseline the percent decrease in reported hot flashes/day on soy was 22% and 26% while on the placebo bar. The effect of the study bar on the intensity of hot flashes is reported in Table 5 which indicates that there was no statistical difference in reported intensity while on either of the bars. There were 1806 days of observational days for recording intensity.

Comparison of endogenous hormone values at baseline, while on the soy bar or while on the placebo bar are presented in Table 6. Compared to baseline the soy bar caused a significant decrease in estradiol ($p=0.003$). This was not seen when the subjects were on the placebo bar. The comparison between the estradiol levels while on the soy versus on the placebo was also statistically significant ($p=0.03$). The data were analyzed using repeated measure regression, using the log scale for the hormone values. Sex-Hormone Binding Globulin (SHBG) was statistically lower while women were on the soy bar compared to baseline ($p=0.0001$). This was also true when women were on the placebo bar compared to baseline ($p=0.02$) but this significance was less and might be due to a carry over effect in those women who received the soy bar first. This will be further explored in later analyses. Compared to the placebo bar, women on the soy bar had statistically higher FSH and LH ($p=0.03$).

Serum phytoestrogen levels in the 7 women who had this analyzed at baseline and while on soy showed significantly higher levels of genistein and daidzein of 19 versus 705 nmol/L for genistein and 11 versus 313 for daidzein. This was significant at the $p=0.0001$ level for genistein but was borderline for daidzein ($p=0.06$). Levels of the phytoestrogens for the 3 samples determined on the placebo bar were statistically lower than during the placebo bar, but they were higher than phytoestrogen levels observed during baseline. This result is due entirely to one of the three samples which had high levels of phytoestrogen and we believe this may indicate some error in sample labeling. We have included all three samples in the placebo group until we have more data on the accuracy on sample identification.

Table 9A contains the data on the correlation between the number of reported hot flashes categorically divided into three groups by hot flash frequency (<1/day, 1-5/day, >5/day). Estrone-sulfate shows a statistically significant decrease with increasing number of hot flashes from 327,

to 239 to 213 ($P=0.02$).

Table 9B indicates that there is a statistically significant decrease in SHBG with increased reporting of hot flashes ($p=0.05$) and a statistically significant increase in FSH with increasing number of hot flashes ($p=0.01$).

Discussion:

It is clear that our study, which contained a large number of women and which had a strong cross-over design failed to show either a decrease in the number or intensity of hot flashes when women were consuming the soy dietary bar with an intake of 45mg of phytoestrogens per day. While the number of reported hot flashes did not diminish when the women were on the soy, their endogenous hormones did show some significant changes. Estradiol did decrease while on the soy compared to baseline ($p=0.003$) and compared to the placebo bar ($p=0.03$). SHBG also decreased on the soy bar compared to the baseline value and the placebo bar. FSH and LH increased only when the soy and placebo bar were compared ($p=0.03$ for each). This indicates that the ingestion of the phytoestrogens did have an impact on the endogenous hormones with a decrease in estrogenic compounds (estradiol) which was further supported by the increase observed in FSH. One possible explanation for a lack of effect could be the level of phytoestrogens used in the intervention. Data in Table 8A is from a study by Adlercreutz et al (Lancet, 1993, 342:1209) that reports the phytoestrogen levels of males in the Japanese population consuming diets high in soy products. The serum phytoestrogen of the Japanese men were lower than we reported in our study population. Table 8B contains data from Brzezinski et al (Menopause, 1997, 4:89) in which they determined serum phytoestrogen levels in women consuming a diet rich in phytoestrogens. They report serum levels of genistein and daidzein that are slightly lower than found in our study group. They, however, did observe a decrease in hot flashes in women while on this diet. In addition they reported lower levels of estradiol, which we also report, and additionally they saw higher levels of SHBG while on the soy diet, which we did not observe. Their diet included tofu, soy milk, miso and ground flax seed. The exact level of genistein and daidzein was not reported but may be closer to 90-100 mg/day. While the dietary intake we used resulted in serum phytoestrogen levels in the range of these two studies, higher levels may be required in order to have an effect on hot flashes.

The analyses of the study data are still not complete, and we plan to look at the reported hot flashes only in the last two weeks of the soy and placebo intervention to determine if reporting at the end of each cycle when, the maximum effect would be expected, would have any effect on the final results. We do not expect to see this, however, from our preliminary look at the data. In addition we have yet to analyze the dietary intake data or the menopausal symptoms questionnaire from the study.

We also plan to carry out a more extensive review of the current literature to determine if other studies have looked at the level of hormones associated with hot flashes besides the original work by Erlik, Meldrum and Judd in 1982 (J Am Coll Obstet. and Gyn, 59:403). The upcoming Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease will also be informative concerning results of other investigators related to the dose levels administered and its variability due to target organ. We expect to send to your office a draft of the manuscript on this study as soon as it is available, which is anticipated in 3-4 months.

Key Research Accomplishments:

- * 45 mg/day of dietary phytoestrogens did not decrease number or intensity of hot flashes compared to the placebo group
- * 45mg/day of dietary phytoestrogens resulted in a decrease in serum estradiol and Sex-Hormone Binding Globulin compared to the baseline data
- * 45 mg/day of dietary phytoestrogens resulted in increased FSH and LH compared to the placebo group
- * 45mg/day of dietary phytoestrogens resulted in serum levels that were higher than that reported in an Asian population.
- * A statistically inverse relationship was found between serum estrone-sulfate and number of hot flashes
- * A statistically direct relationship was found between follicle stimulating hormone and number of hot flashes

Reportable Outcomes:

1. Two publications are expected from this research.
2. Three abstracts and two presentations have resulted from this work:
See abstracts in Appendix and presentations where noted

Conclusions:

An intake of dietary phytoestrogens of 45 mg/day do not result in a decrease in the number or intensity of hot flashes reported by women compared to a placebo control. Both the soy dietary supplement and the placebo dietary supplement resulted in a 22% and 26% decrease in the number of hot flashes reported by the women. However, endogenous hormone levels were changed by the intake of the dietary soy supplement which included: a decrease in estradiol ($p=0.003$), a decrease in Sex-Hormone Binding Protein, SHBG, ($P=0.0001$) compared to baseline and an increase in follicle-stimulating hormone compared to the placebo ($p=0.03$). The determination of serum phytoestrogens genistein and daidzein, indicated that the elevation observed in a sub-set of the women ($N=7$) while on the soy bar was higher than that reported in Asian men on their typical diets or in a study that reported an effect of soy and phytoestrogens on number of hot flashes. An inverse association was found between estrone-sulfate ($p=0.02$) and the number of reported hot flashes while a direct association was observed with follicle stimulating hormone ($p=0.01$).

The practical significance of this work indicates that either soy dietary supplements do not have an impact on menopausal symptoms or that levels of intake higher than that consumed by the Asian population may be necessary to see an effect. Many women are seeking alternatives to hormone replacement therapy (HRT) for hot flashes and the efficacy of using soy products or phytoestrogens is still unclear. An intake of 45 mg/day which allows serum levels of phytoestrogens to rise to levels equal to that reported in the Japanese population or in other studies that have reported an effect of soy were not duplicated in our study. Intake of phytoestrogens at 45 mg/day were capable, however, of decreasing serum estrogens and SHBG which may be protective in reducing exposure to risk for breast cancer.

Table 2: Basic Socio-Demographic Characteristics of Intervention Subjects by Number of Hot Flashes/Day

Characteristic	(% in each category)		P-Value
	1-5/Day (N = 27)	5+ /Day (N = 49)	All (N = 76)
<u>Marital Status</u>			
Currently Married	69.5	45.8	54.0
Not Currently Married	30.8	54.2	45.6
<u>Education</u>			
≤ 12 Years	18.5	26.5	23.7
> 12 Years	81.5	73.5	77.3
<u>Ever Pregnant</u>	77.8	89.8	85.5
<u>Ever Breast-Fed (If Pregnant)</u>	47.6	44.2	45.3
<u>History of Irregular</u>	48.2	64.6	58.7
<u>Menstrual Periods</u>			
Ever Used Oral Contraceptives	74.1	70.8	72.0
Ever Used HRT for Menopause	33.3	37.5	36.1
<u>Alcohol Use</u>	48.2	53.2	51.4
<u>Current Smoker</u>	8.3	6.3	6.9

by X²

Fisher's Exact

Table 3: Number of Hot Flashes by Bar Type^a

Time Period	# of Hot Flashes (CI) ^b	# of Days	P ₁ ^c	P ₂ ^d
Baseline	6.6 (5.9, 7.4)	973	--	--
Low Bar	5.2 (4.5, 5.9)	6369	0.0001	0.32
Placebo Bar	4.9 (4.3, 5.7)	6278	0.0001	--

Poisson Model

CI = Confidence Interval

P₁ = p-value for comparison with baseline

P₂ = p-value for comparison with placebo bar

Table 4: Percent Change in Menopausal Symptoms by Bar^a

	% Change (CI) ^b	P-Value
Comparison to Baseline		
•Soy Bar	-22% (-30, -12)	0.0001
•Placebo Bar	-26% (-35, -15)	0.0001
Comparison to Placebo Bar		
•Soy Bar	+5% (-5, +16)	0.32
Poisson Model		
CI = Confidence Interval		

Table 5: Effect of Bars on Hot Flash Intensity
Scale 1 (Low) - 5 (High)

	Intensity Mean (SE)	P ^a	P ^b
baseline	2.31 (0.09)	--	--
oxy Bar	2.19 (0.10)	0.22	0.96
placebo Bar	2.18 (0.11)	0.21	--

P₁ = p-value of comparison of intensity with baseline value

P₂ = p-value of comparison of intensity with placebo value

N = 1806 days of reporting; N = 79 women

Table 6: Effect of Bars on Hormone Levels

	Baseline		Soy Bar		Placebo Bar		P ¹		
	Mean	(SE Range)	Mean	(SE Range)	P ¹	P ²			
Subjects	79		77		78				
Measurements	135-136		132		131				
Testosterone (pg/mL)	26.8	(25.1, 28.6)	25.4	(24.1, 26.8)	.17	.17	26.6	(25.1, 28.1)	.85
Estradiol (pg/mL)	24.6	(23.0, 26.3)	20.2	(19.2, 21.3)	.003*	.03*	23.5	(21.9, 25.3)	.47
Free Estradiol (pg/mL)	0.34	(0.32, 0.37)	0.31	(0.29, 0.33)	.08	.11	0.3	(0.32, 0.36)	.60
Testosterone S ₀₄ (pg/mL)	214.5	(200.6, 229.3)	199.2	(186.8, 212.5)	.17	.70	208.3	(193.5, 224.4)	.36
Androstenedione (ng/mL)	0.82	(0.78, 0.85)	0.80	(0.76, 0.84)	.67	.67	0.79	(0.75, 0.83)	.45
Dehydroepiandrosterone (ng/mL)	0.11	(0.10, 0.12)	0.10	(0.09, 0.11)	.24	.22	0.09	(0.08, 0.11)	.02*
IGFBP-1 (µg/dL)	43.2	(40.7, 45.8)	37.4	(35.3, 39.6)	.0001*	.06	39.6	(37.3, 42.1)	.02*
IGFBP-3 (ng/mL)	64.7	(60.6, 69.0)	69.8	(66.1, 73.8)	.08	.03*	62.4	(58.1, 67.0)	.73
IGFBP-5 (ng/mL)	36.6	(33.8, 39.7)	41.2	(39.0, 43.6)	.09	.03*	36.5	(33.8, 39.4)	.87

* = p-value for comparison with baseline

† = p-value for comparison of soy bar with placebo bar

Based on repeated measure regression with empirical variance, using the log scale for hormone values

Statistically significant

Table 7: Serum Phytoestrogen Levels

Measurement number	Baseline N = 7	Soy N = 7	Mean (SE Range) P ¹	Placebo N = 3	P ¹
Genistein (mol/L)	19 (14, 26)	705 (625, 794)	0.0001*	67 (31, 147)	0.0001*
Daidzein (mol/L)	11 (8, 15)	313 (277, 355)	0.06	50 (24, 108)	0.04*

* = P-value from repeated measure regression on log scale with comparison to baseline.

Table 8A: Serum Isoflavoids in Japanese Men (N = 14)

Compound	Geometric Mean	(95% CI)
Genistein (nmol/L)	270	(116 - 652)
Daidzein (nmol/L)	107	(47.4 - 237)

Adlercreutz, et al. 1993, Lancet: 342:1209

**Table 8B: Serum Concentrations of Phytoestrogens
(nmol/L) (Mean, SEM)**

	Baseline	Phytoestrogen-rich Diet
Genistein	16.63 (3.58)	364.0 (60.76)
Daidzein	15.01 (7.15)	178.0 (33.08)

Phytoestrogen-rich diet: tofu, soy milk, miso, ground flax seed
 Wozniakowski, et al., Menopause, Vol. 4:89, 1997

Table 9 : Association between Baseline Hormone Levels and Reported Number of Hot Flashes/Day

	< 1/day		1-5/day		> 5/day		P from regression on hot flashes
	Mean	(SE Range)	Mean	(SE Range)	Mean	(SE Range)	
acts		32		27		48	
measurements		45		48		82	
estrone (pg/mL)	20.3	(18.0, 22.8)	31.6	(28.3, 35.3)	24.7	(22.8, 26.9)	.54
estradiol (pg/mL)	19.5	(17.3, 22.0)	29.0	(26.1, 32.2)	22.2	(20.3, 24.2)	.79
estrone (pg/mL)	0.26	(0.22, 0.29)	0.40	(0.35, 0.45)	0.31	(0.28, 0.34)	.28
estrone (pg/mL)	327.6	(292.2, 367.3)	239.3	(212.7, 269.3)	213.0	(196.8, 230.5)	.02*
estrone (ng/mL)	0.69	(0.62, 0.77)	0.87	(0.81, 0.93)	0.81	(0.76, 0.87)	.20
estrone (ng/mL)	0.09	(0.08, 0.11)	0.13	(0.11, 0.15)	0.10	(0.09, 0.11)	.86
estrone (μg/dL)	45.1	(41.9, 48.5)	48.4	(44.5, 52.7)	39.8	(36.7, 43.1)	.05*
estrone (mIU/mL)	43.6	(36.3, 52.3)	56.0	(48.5, 64.7)	71.5	(67.1, 76.2)	.01*
estrone (mIU/mL)	28.7	(24.2, 34.0)	31.7	(25.8, 38.9)	39.2	(36.8, 41.9)	.06

* p < 0.05 on repeated measures regression with empirical variance, using the log scale for hormone values
 † statistically significant

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2. Brzezinski A, Adlercreutz H, Shaoul R, Rosler A, Shmueli A, Tanos V, and Schenker JG. Short-term Effects of Phytoestrogen-rich Diet on Postmenopausal Women. *Menopause: The Journal of the North American Menopause Society* 1997; 4:89-95.

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APPENDIX

- Appendix 1: Presentation: Effect of a Dietary Soy Bar on Menopausal Symptoms, Second International Conference on Soy and Health, Brussels, Belgium, 9/15-9/18/96
- Appendix 2: Poster Sessions: Dietary Soy Supplement and Menopausal Hormones and Hot Flashes, Era of Hope, the Dept of Defense Breast Cancer Research Program Meeting, Washington, D.C., 10/31-11/4/97, Poster # 500-W
- Appendix 3: Presentation: Dietary Soy Supplement and Menopausal Hormones and Hot Flashes, 3rd International Symposium on the Role of Soy in Preventing Chronic Disease, Washington, D.C., 10/31-11/3/99

PRESENTATION:

SECOND INTERNATIONAL CONFERENCE ON SOY AND HEALTH

Brussels, Belgium

September 15-18th, 1996

Effect of a Dietary Soy Bar on Menopausal Symptoms

M.N. Woods, R. Senie, D. Spiegelman, A. LaBrode, and F. Kronenberg

Background: Epidemiological data indicated that Asian women reported lower levels of hot flashes compared to Western women. The high consumption of soy products by the Asian women, which is known to contain high levels of phytoestrogens (plant estrogens), was considered as an explanation for this difference in experiencing of hot flashes. No scientific study had investigated the relationship between soy intake, serum hormones, and number of hot flashes.

Methods: Women, ages 44-57, reporting daily menopausal symptoms of hot flashes were recruited for the study. Screening records documented the number of hot flashes each day and women with low (<2 /day) versus high (>5 /day) levels of hot flashes were identified. Blood samples were collected to verify menopausal status by FSH and LH and to determine baseline estrogen levels. Women experiencing high symptomatology were randomized into either a soy or placebo bar study group. Two dietary soy bars, the daily allotment, contained 40 mg of phytoestrogens. The women consumed the bars for a minimum of 12 weeks. Number of daily hot flashes were recorded for the entire time period and the time of each event was recorded during one week. Blood was obtained during week 12 for the determination of FSH, LH, E_1 , E_2 , E_1-SO_4 , free E_2 , Androstenedione, Testosterone and Sex-Hormone-Binding-Globulin.

Results: Preliminary data indicates great within person variability in menopausal symptoms on a daily and monthly basis. The range of hot flashes reported in the women with high symptomatology was 4-18/day. The difference in reported number of symptoms between the baseline and soy treatment indicated a small decrease in menopausal symptoms while on the soy (-1.7 hot flashes/day ± 3.9 , SD).

Conclusions: Great variability exists in the experiencing of hot flashes in menopausal women. Soy may have a small effect on the level of reported hot flashes.

Key Words:

Menopause

Phytoestrogen

Hormones

Menopausal hot flashes

POSTER SESSIONS:

ERA OF HOPE

The Department of Defense Breast Cancer Research Program Meeting
Washington, D. C.
October 31-November 4, 1997
Poster # 500-W

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Estrogen exposure is generally considered a risk factor for breast cancer. This is most obviously evidenced by the use of the antiestrogen, tamoxifen, for treatment of breast cancer. Medical advice to women who are at increased risk for breast cancer, is to avoid use of hormone replacement therapy when they reach menopause, leaving them with few options to deal with menopausal symptoms of hot flashes and night sweats. Numerous alternative health therapies have been proposed to help alleviate these symptoms, with little scientific data to support their use. Recent interest in soy products to alleviate symptoms of menopause is due to the low level of hot flashes reported by Asian women and their high intake of soy products, which are known to contain phytoestrogens. Phytoestrogens are known to bind to estrogen receptors and at high serum levels, can displace the more active endogenous estrogens.

Our study was designed to determine if a soy supplement with 45 mg/day of phytoestrogens would decrease the number and intensity of hot flashes and night sweats in menopausal women (45-58 years of age) reporting > 5 hot flashes/day.

Women at increased risk for breast cancer, due to family history, and with > 5 hot flashes per day were recruited to join a 7 month, double blind, cross-over study using a soy dietary supplement bar and a placebo bar to determine the effect of soy on the number of menopausal symptoms. A population of N=100 women was sought. Women filled out a menopausal questionnaire and kept a daily diary on their symptoms for two weeks at baseline and provided blood for the determination of hormones and gonadotrophins. They were then randomized into the soy or placebo supplement group for a period of 12 weeks. Daily records on symptoms were kept and a blood sample was obtained at the end of the 12 weeks. One month of wash-out was followed by the alternate bar for a second 12 weeks and repeated data collection. A control group of women who report <2 hot flashes/day were also recruited for a baseline period of two weeks to obtain data on hot flashes and hormone levels in women who were not experiencing many symptoms of menopause. Serum levels of phytoestrogens will be determined in a sub-sample of women, N=12, to determine the level achieved by the soy supplement to compare to an Asian population and document the serum level needed to achieve a biological effect.

Recruitment of women into the study was hampered due to recent data which suggested that women at increased risk for breast cancer due to family history could take hormone replacement therapy (HRT) and not increase their risk of breast cancer. This has resulted in greater number of women choosing HRT than previously. We have used extensive recruiting in newspapers and radio to reach our targeted population and currently have enrolled N=68 women into the study protocol. Almost half of this population has been recruited during March and April, 1997. This group will complete the seven month protocol in August and September.

Data are analyzed to determine changes in reported number and intensity of hot flashes within each woman on the soy versus placebo group as well as group differences of number of symptoms on the soy versus placebo bar. Hormone levels on the soy versus placebo bar were determined to correlate symptoms with hormone and gonadotrophin levels. Comparison of hormone values in women reporting high versus low levels of symptoms are carried out to determine if endogenous hormone levels are correlated to the number and intensity of hot flashes. The daily symptoms diary collected for six months was also used to determine within person and between person variability in this population of women chosen to characterize women with elevated number of daily symptoms ($>5/\text{day}$). Little data is available on the natural history of hot flash symptoms and our data will provide an opportunity to observe variability over a 3-7 month time period.

Key words: Breast Cancer, Menopause, Hot Flashes, Hormones, Soy

U.S. Army Medical Research and Materiel Command under DAMD-1794C4120

PRESENTATION:

Dietary Soy Supplement and menopausal Hormones and Hot Flashes
M. Woods, R. Senie, A. LaBrode, S. Gorbach

Third International Symposium on the Role of Soy in Preventing and Treating
Chronic Disease
Washington, D.C.
October 31st -November 3, 1999

Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease

Sunday, October 31–Wednesday, November 3, 1999, Omni Shoreham Hotel, Washington, DC, USA

ABSTRACT FORM

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Presentation preference: ☐ Paper ☒ Poster

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Dietary Soy Supplement and Menopausal Hormones & Hot Flashes

Author(s):

(List principal author first; underline presenter's name if different from principal author.)

Company(ies)/Institution(s):

Margo Woods, Rubie Senie, Ann LaBrode and Sherwood Gorbach
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Abstract:

A 7 month, double blind, cross-over study was designed to determine if a soy supplement containing 45 mg/day of phytoestrogen would decrease the number and intensity of hot flashes and night sweats in menopausal women (45-58 years of age) reporting ≥ 5 hot flashes/day.

An alternative to hormone replacement therapy (HRT) for the alleviation of hot flashes would be welcomed by the medical community and many patients who do not choose to use HRT.

Eighty-five women completed the protocol that started with two weeks of baseline data, recording menopausal symptoms, and collecting blood for the determination of baseline hormones and gonadotrophins. Women were randomized into a soy or placebo supplement group for a period of 12 weeks. Daily record on symptoms were kept and a blood sample obtained at the end of the 12 weeks. One month of wash-out was followed by the alternative bar for a second 12 weeks and repeated data collection. Serum levels of phytoestrogens were determined in a sub-sample of the women, $N=12$, to determine the serum levels achieved on the soy supplemented compared to reported levels in Asian women. A control group of women ($N=55$) were recruited that reported <1 hot flash/day for a baseline period of two weeks to obtain data on hot flashes and hormone levels and gonadotrophins in women in the same age category and stage of menopause who were experiencing a low level of hot flash symptoms.

Data are currently being analyzed to determine the number of hot flashes reported while on the soy versus placebo bars, the change in hot flashes from baseline for each of the interventions plus reported changes in intensity of symptoms. Hormone and gonadotrophin levels at baseline and during each intervention are also being evaluated. Baseline hormone values between women reported high levels of hot flashes will be compared to those reporting a low level of symptomatology. Variability in reported hot flashes will also be analyzed since little data is available on the stability of daily reported hot flashes and night sweats.

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